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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/053,975 | 01/18/2002 | Limin Li | STAN-216 | 5176 |

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| EXAMINER | |
|---|---|
| FETTEROLF, BRANDON J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| **Advisory Action Before the Filing of an Appeal Brief** | **Application No.** 10/053,975 | **Applicant(s)** LI ET AL. | |
|---|---|---|---|
| | **Examiner** Brandon J. Fetterolf, PhD | **Art Unit** 1642 | |

***--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --***

THE REPLY FILED 31 October 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,4-6 and 43*.
   Claim(s) withdrawn from consideration: *7-16, 22-25, 31-32, 37-42 and 44-45*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

***Response to the Amendment***

The Amendment filed on 10/31/2005 in response to the previous Final Office Action (06/29/2005) is acknowledged, but has not been entered because the amendment does not put the instantly filed application in further condition for Allowance.

Claims 1, 4-16, 22-25, 31-32 and 37-45 are currently pending.

Claims 7-16, 22-25, 31-32, 37-42 and 44-45 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 1, 4-6 and 43 are currently under consideration.

**The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.**

**Rejections Maintained:**

Claims 1, 4-6 and 43 **remain** rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record in the prior Office Actions (01/26/2005, pages 4-6 and 06/29/2005, pages 2-3) and for the reasons set forth below.

In reference to the previous action which held that the specification only reasonably conveys antibodies that bind to one species of polypeptide comprising a ubiquitination domain referred to as human TSG101 consisting of the amino acid sequence set forth in SEQ ID NO: 1, but not antibodies to any functional fragment thereof, Applicant's assert (Page 8) that the specification provides reduction to practice of a representative number of species (see, for example, the fragments listed on page 24, last paragraph of the specification), discloses functional characteristics shared by all of the species and a correlation between function and structure. For example, Applicants submit that the specification (page 12, lines 3-4) recites "a functional fragment of an ubiquitination-conjugase-like Ubc domain refers to any fragment of the Ubc domain that regulates ubiquitination." As such, Applicants assert that the functional characteristics shared by all of the species

encompassed by the claimed genus "...ubiquitination-regulating domain, or a functional fragment thereof..." is the ability to regulate ubiquitination. Moreover, Applicants point to page 26 of the specification which discloses a method by which one can determine which fragments of a ubiquitination-regulating domain regulates ubiquitination. Thus, Applicants contend that the specification teaches one of skill in the art how to identify functional fragments of an ubiquitination-regulating domain. Furthermore, Applicants argue that they have identified a correlation between function and structure as shown in Figure 3(a) of the speciation.

These arguments have been carefully considered, but are not found persuasive.

In response to Applicants arguments that the specification provides reduction to practice of a representative number of species (see, for example, the fragments listed on page 24, last paragraph of the specification), discloses functional characteristics shared by all of the species and a correlation between function and structure, the Examiner concedes that the specification provides the complete sequence of the ubiquitination-regulating domain of human TSG101 (page 24, last paragraph) and deletion fragments of human TSG101 (Figure 3A). However, the specification does not appear to provide a written description for any and/or all functional fragments of a polypeptide comprising an ubiquitination-regulating domain comprising the amino acid sequence of SEQ ID NO: 1. In this instance, the transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). Thus, while one of skill in the art may reasonably convey that Applicants were in possession of the claimed genus of polypeptide consisting of an ubiquitination-regulating domain or function fragment thereof of a human TSG101 protein consisting of the amino acid sequence of SEQ ID NO: 1, wherein the fragment regulates ubiquitination, Applicants have not reasonably conveyed that they were in possession of the presently claimed genus. Moreover, while Applicants contend that the specification teaches one of

skill in the art how to identify functional fragments of an ubiquitination- regulating domain, Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115). As such, the specification describing to one of skill in the art how to identifying function fragments does not reasonably convey that Applicants were in possession of the claimed genus.

Claims 1, 4-6 and 43 **remain** rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (IDS, US 5,891,668, 1999) or Brie et al. (US 5,892,016, 1999) for the reasons of record in the prior Office Actions (01/26/2005, pages 6-8 and 06/29/2005, pages 3-6) and for the reasons set forth below.

In reference to the previous action which held that Li et al. (pages 6-7) teaches antibodies which specifically bind to the coiled domain, leucine zipper and proline rich domains of TSG101 and Brie et al (page 7-8) teaches antibodies to a purified protein having 100% sequence identity to the amino acid sequence set forth in SEQ ID NO: 1, Applicants assert that Li et al. and Brie et al. each describe a genus of antibodies that bind to the full length TSG101. In contrast, Applicants contend that the present invention discloses a species of that genus (i.e., antibodies that bind specifically to the ubiquitination-regulating domain of human TSG101). As such, Applicants submit that a genus does not always anticipate a claim to a species within the genus, if the species is not specifically taught (See MPEP, 2131.02). Therefore, Applicants argue that since neither Li et al. nor Brie et al. teach or suggest the existence of a ubiquitination-regulating domain of human TSG101, neither of these references teach or suggest an antibody that binds to this region. Furthermore, Applicants assert that binding to the ubiquitination-regulating domain is not an inherent characteristic of the antibodies of Li et al. or Brie et al.. Applicants further contend that inherency may not be established by probabilities or possibilities and that the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient. In re Rijckaert, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) and MPEP 2112 IV. "[T]he examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristics necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). As such, Applicants

contend that due to the protein folding, ect., antibodies developed to the full length TSG101 may not necessarily bind to the ubiquitination-regulating domain.

These arguments have been carefully considered, but are not found persuasive.

In response to Applicants arguments that species does not anticipate a species, the Examiner agrees that a genus disclosed in the prior art does not always anticipate species as outlined in the MPEP 2131.02. However, Applicants have not provided a patentable difference between the antibody presently claimed and the ones disclosed in the prior art. In the instant case, the claims are drawn to an isolated antibody that binds to a polypeptide comprising (emphasis added) an ubiquitination-regulating domain, or a functional fragment thereof, of a human TSG101 protein comprising (emphasis added) the amino acid sequence recited in SEQ ID NO: 1. The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). Thus, there does not appear to be a patentable difference between an antibody which binds to a polypeptide fragment (100% identical from amino acids 11 to 390 of SEQ ID NO: 1) of the amino acid sequence recited in SEQ ID NO: 1 (Li, US 5,891,668, see sequence comparison) or an antibody which binds to a polypeptide that is 100% identical (see sequence comparison) to a polypeptide comprising the amino acid sequence recited in SEQ ID NO: 1, wherein the ubiquitination-regulating domain may comprise amino acid residues 50-140, 1-140 or 140-250 of SEQ ID NO: 1. With regard to Applicants contention that binding to the ubiquitination-regulating domain is not an inherent characteristic of the antibodies of Li et al. or Brie et al., the Examiner recognizes that inherency may not be established by probabilities or possibilities and that the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient. However, the claims are drawn to an isolated antibody that binds to a polypeptide comprising (emphasis added) an ubiquitination-regulating domain, or a functional fragment thereof,

of a human TSG101 protein comprising (emphasis added) the amino acid sequence recited in SEQ ID NO: 1. The prior art teaches an antibody which binds to a polypeptide (100% identical from amino acids 11 to 390 of SEQ ID NO: 1) comprising a ubiquitination-regulating domain comprising the amino acid sequence recited in SEQ ID NO: 1 (Li, US 5,891,668, see sequence comparison) and an antibody which binds to a polypeptide that is 100% identical (see sequence comparison) to a polypeptide comprising a ubiquitination-regulating domain comprising the amino acid sequence recited in SEQ ID NO: 1, wherein the ubiquitination-regulating domain may comprise amino acid residues 50-140, 1-140 or 140-250 of SEQ ID NO: 1. Thus, the claimed antibody appears to be the same as the prior art. As stated in the prior Office Action (pages 7 and 8), the office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. (emphasis added) See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). Therefore, amended claims 1, 4 and 6 remain rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (IDS, US 5,891,668, 1999) and claims 1, 4-6 and 43 remain rejected under 35 U.S.C. 102(b) as being anticipated by Brie et al. (US 5,892,016, 1999)

Therefore, NO claim is allowed

**All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
11/22/05